Grading, therapy monitoring, and predicting outcome of glioma using perfusion MR imaging

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I. Gliomas

- Most common primary brain tumor
- Grade I-IV: WHO classification (revised in 2000) based on histologic features
- Grade I: Biologically indolent, "benign" brain tumors (ex. Pilocytic astrocytoma, subependymal giant cell astrocytoma, pleomorphic xanthoastrocytoma)
- Grade II-IV: Fibrillary astrocytomas most common, followed by oligodendrogliomas and oligoastocytomas (a.k.a. mixed gliomas)
- Grade IV Glioblastoma Multiforme (GBM): Most common gliomas, most aggressive biologically, highly vascular and necrotic
- Standard Imaging: MR imaging with Gd-DTPA (perfusion, diffusion, proton spectroscopy as optional imaging)
- Standard Treatment
    - Grade III & IV Gliomas: Surgical resection followed by external beam radiation therapy (50-60 Gy for 6 weeks) and chemotherapy (temozolamide most widely used)
    - Grade II Gliomas: Surgical resection initially & radiation therapy and/or chemotherapy at recurrence or progression
- Prognosis (Average survival in months)
    - Grade IV: 12-18 months
    - Grade III: 3-5 years
    - Grade II: 10-15 years

II. Types of Perfusion MR Imaging

- Endogenous contrast agent: Arterial Spin Labeling (ASL)
    - No exogenous contrast agent
    - Absolute cerebral blood flow
- Exogenous contrast agent (Gd-DTPA)
    - T2 or T2* dynamic susceptibility-weighted contrast-enhanced (DSC) "perfusion" MR imaging:
        - Relative cerebral blood volume (rCBV), blood flow, and transit time
    - T1-weighted dynamic contrast-enhanced (DCE): "Permeability" MR imaging"
        - Extracellular extravascular space, blood flow, cerebral blood volume (CBV), permeability surface product (^{Ktrans})

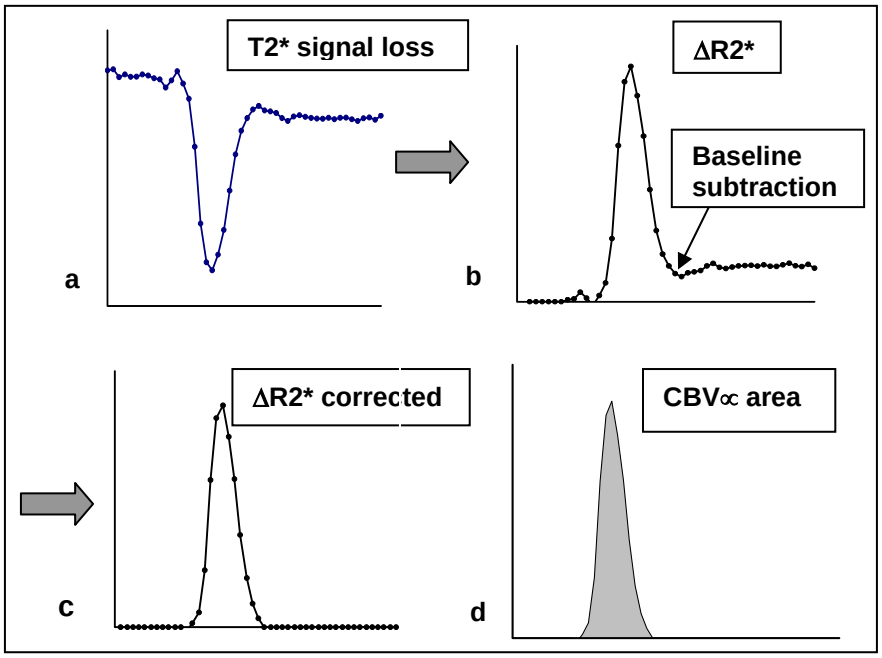
III. Fundamentals of DSC Perfusion MR imaging

- Rapid repeated imaging of multi-slice sections of the brain before, during, and after bolus injection of Gd-DTPA
- Compartmentalization of intravascular Gd-DTPA before it reaches interstitial space
- T2* signal loss due to Gd-DTPA, the susceptibility contrast, is translated into T2* relaxivity contrast, ΔR2*
- Fitting of ΔR2* signal intensity time curve allow measurement of area under the curve, which is proportional to cerebral blood volume (CBV)
- Steps involved in CBV calculation from DSC MR imaging data is illustrated in Figure 1.

- In case of blood-brain barrier breakdown as in some malignant gliomas or metastasis, signal recovery to baseline does not occur due to Gd-DTPA leakage, hence CBV calculation can be erroneous
- Alternate variables such as peak height (PH) or percent signal recovery (PSR) can be derived from ΔR2* curve as shown in Figure 2.

Figure 1. CBV Data Analysis

a. Obtain curves of T2* signal intensity against time (Figure 1a).
b. Estimate mean pre-contrast signal intensity (S_0) from ten data points acquired before arrival of the bolus. Exclude the first 3-4 images during which the steady-state MR signal is established.
c. Calculate $\Delta R2^*$ and apply baseline subtraction to the ΔR2 curve (Figure 1b & 1c).
d. Calculate the area under the fitted curve (Figure 1d).



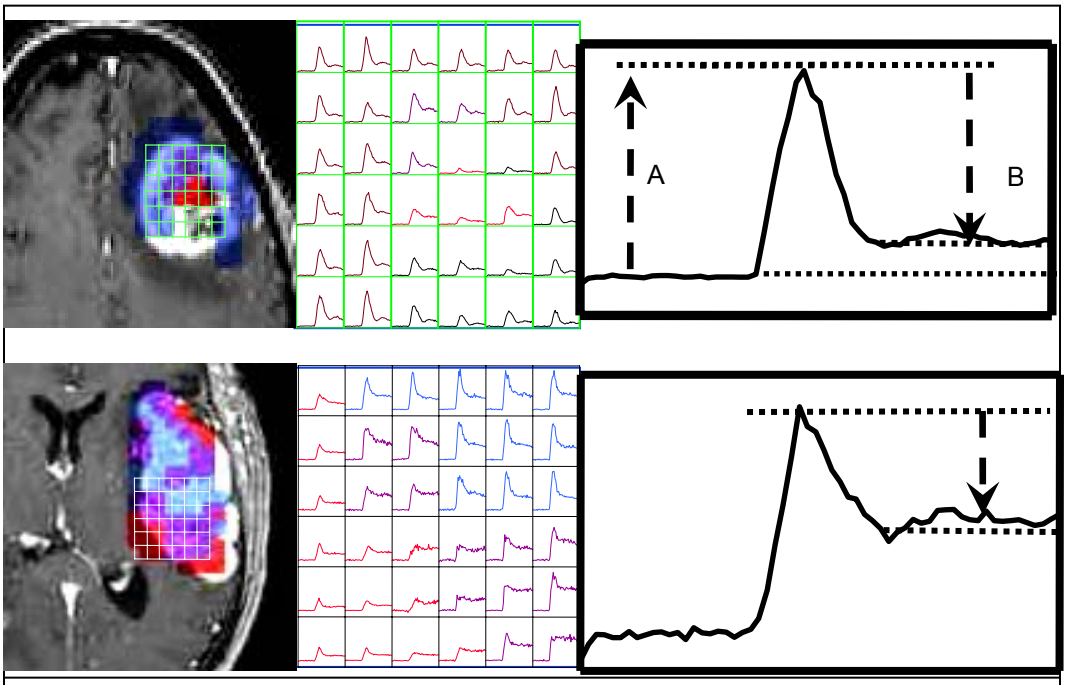


Figure 2. ΔR2* curve analysis in two different patients with brain tumor. Top-Malignant glioma; bottom-dural based metastasis. Peak height (A) is the maximum signal change during first-pass of Gd-DTPA; Percent signal recovery (PSR) is percentage of signal recovery to the baseline at the end of bolus and is represented by B/A x 100%. Metastasis has decreased PSR due to leaky capillaries.
(*Figure courtesy of Janine M. Lupo*)

IV. Glioma Grading based on DSC Perfusion MR imaging

- rCBV most commonly used; higher the tumor grade, greater the rCBV
- Exception: Oligodendroglioma—low and high grade tumors both tend to have increased vascularity on histology; rCBV cannot reliably differentiate between the two
- rCBV based gliomas grading should be limited to fibrillary astrocytomas

V. Glioma Grading based on Permeability MR imaging

- K^{trans} most commonly used but CBV has been used
- Strong independent relationships between both K^{trans} & CBV and histologic grade in gliomas
- K^{trans} has higher discriminative power in distinguishing between grade II (low-grade) and grade III+IV (high-grade) than between grade III and grade IV

VI. Therapy monitoring based on Perfusion MR imaging

- Serial tumor rCBV measurements during therapy can predict early response to therapy
- Interval increase tumor rCBV tend to represent treatment failure

Table 1. Summary of various types of perfusion MR imaging

	Gd-DTPA	Perfusion MR Variables	Strengths	Weaknesses
ASL	No	CBF	No IV contrast Absolute measures	Long imaging time; no CBV; 3T or higher; motion
T1-DCE	Yes	fPV K^{trans} EES Initial slope Time to peak Area under curve	Higher spatial resolution No susceptibility artifact	Longer scan time
T2-DSC	Yes	rCBV rCBF MTT	Less distortion Fast; multislice	Multiple dose of Gd-DTPA
T2*-DSC	Yes	rCBV rCBF MTT	Fast; multislice Single dose Gd-DTPA High SNR	Geometric distortion

ASL: Arterial Spin Labeling
DCE: Dynamic contrast-enhanced Permeability MR imaging
DSC: Dynamic susceptibility-weighted contrast-enhanced Perfusion MR imaging
CBF: Cerebral Blood Flow
fPV: Fractional Plasma Volume
Ktrans: Volume transfer coefficient
EES: Extravascular Extracellular Space

References

Glioma and angiogenesis

Kleihues P, Soylemezoglu F, Schauble B, Scheithauer BW, Burger PC. Histopathology, classification, and grading of gliomas. Glia 1995:15:211-221

Wesseling P, Ruiter DJ, Burger PC. Angiogenesis in brain tumors; pathobiological and clinical aspects. J Neurooncol 1997;32:253-265

Plate, K. H.
Mennel, H. D. Vascular morphology and angiogenesis in glial tumors. Exp Toxicol Pathol 1995;47:89-94

Dynamic susceptibility-weighted contrast-enhanced MR imaging

RosenBR, Belliveau JW, Vevea JM, Brady TJ. Perfusion imaging with NMR contrast agents. Magn Res Med 1990;14:249-265

Aronen HJ, Gazit IE, Louis DN, et al. Cerebral blood volume maps of gliomas: comparison with tumor grade and histologic finding. Radiology 1994;191:41-51

Knopp EA, Cha S, Johnson G, et al. Glial neoplasms: dynamic contrast-enhanced T2*-weighted MR imaging. Radiology 1999;211:791-798

Lupo JM, Cha S, Chang SM, Nelson SJ. Dynamic susceptibility-weighted perfusion imaging of high-grade gliomas: characterization of spatial heterogeneity. AJNR Am J Neuroradiol 2005;26:1446-1454

Cha S, Knopp EA, Johnson G, Litt A, Glass J, Gruber ML, Lu S, Zagzag D. Dynamic contrast-enhanced T2-weighted MR imaging of recurrent malignant gliomas treated with thalidomide and carboplatin. AJNR Am J Neuroradiol 2000;21:881-890

Dynamic contrast-enhanced T1-weighted permeability imaging

Tofts PS, Kermode AG. Measurement of the blood-brain barrier permeability and leakage space using dynamic MR imaging. 1. Fundamental concepts. Magn Reson Med 1991;17:357-367

Tofts PS. Modeling tracer kinetics in dynamic Gd-DTPA MR imaging. J Magn Reson Imaging 1997;7:91-101

Roberts HC, Roberts, TP, Brasch RC, Dillon WP. Quantitative measurement of microvascular permeability in human brain tumors achieved using dynamic contrast-enhanced MR imaging: correlation with histologic grade. AJNR Am J Neuroradiol 2000;21:891-899

Patankar TF, Haroon HA, Mills SJ, Baleriaux D, Buckley DL, Parker GJ, Jackson A. Is volume transfer coefficient (K^{trans}) related to histologic grade in human gliomas? AJNR Am J Neuroradiol 2005;26:2455-2465